Calcifying pseudoneoplasms of the neural axis

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During the past 36 years, we have encountered 14 cases of a tumefactive lesion occurring in the neural axis. The literature concerning this type of lesion is sparse; Rhodes and Davis,1 Jun and Burdick,2 and Dahlin and Unni3 have described similar cases. The usually good prognosis of the affected patient makes it important to recognize this entity.

Summary of Cases

Clinical Material

The 14 patients with calcifying pseudotumor of the neural axis reported here included five who were treated at the Mayo Clinic between 1950 and 1986 (Table 1). Clinical histories and microscopic slides were examined in all five cases and in three of the cases radiographs were available for evaluation. Review of the patients' charts supplied follow-up information for all five patients. The nine other patients were referred to us for consultation between 1954 and 1986. Clinical histories and microscopic slides were available for all nine cases and radiographs were available for six. Follow-up information was procured in seven cases by correspondence with the referring physicians. Three other cases referred for consultation were excluded because a microscopically identical calcifying pseudotumor was found in a location other than the neural axis. These cases will be mentioned in the discussion.

This series consisted of nine males and five females, ranging in age at the time of diagnosis from 12 to 68 years (Fig. 1). All decades from the second through the seventh were represented. Ten of the patients were between 30 and 60 years of age.

Anatomical Distribution of Lesions

The lesion was present in the frontal lobe in one patient (Case 6) and in the cerebellar tonsil in another (Case 3). In four patients (Cases 1, 2, 7, and 8) tumefactions were located in the soft tissue adjacent to the base of the brain, and all four were associated with bone abnormalities. Bone involvement was very extensive in two of these four cases, and in one of these (Case 7) autopsy showed that the right sphenoid, the ethmoid, the sella turcica, the occipital bone, and the foramen magnum were invaded by the lesion. In the other (Case 1), the pyramid of the left temporal bone, the sphenoid, the jugular canal, the foramen magnum, the naso-oral pharynx, and the vertebral artery were involved. Of the other two patients with bone abnormalities, one (Case 2) had involvement of the skull at the foramen magnum and the other (Case 8) had invasion of the skull at the jugular foramen.

The remaining eight lesions were located along the spinal cord: three at the cervical, two at the thoracic, and three at the lumbar level. These lesions involved
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TABLE 1
Clinical summary of patients with calcifying pseudotumor of the neural axis

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex &amp; Age (yrs)</th>
<th>Symptoms &amp; Duration</th>
<th>Location of Lesion</th>
<th>Type of Treatment</th>
<th>Follow-Up Results &amp; Period*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M, 31</td>
<td>severe headache &amp; hoarseness (4 mos), jugular foramen syndrome</td>
<td>lt cerebellopontine angle, jugular foramen, vertebral canal, oropharynx</td>
<td>intralesional excision; debulking procedure 3 yrs later for recurrence</td>
<td>died of cerebrovascular accident (13 yrs after 1st treatment)</td>
</tr>
<tr>
<td>2</td>
<td>M, 50</td>
<td>rt neck &amp; occipital area pain (23 yrs)</td>
<td>foramen magnum</td>
<td>debulking procedure</td>
<td>NED (3 yrs 6 mos)</td>
</tr>
<tr>
<td>3</td>
<td>M, 48</td>
<td>rt 11th cranial nerve paralysis (&quot;long time&quot;)</td>
<td>rt cerebellar tonsil, spinal accessory nerve involvement</td>
<td>wide excision</td>
<td>NED (19 yrs)</td>
</tr>
<tr>
<td>4</td>
<td>M, 23</td>
<td>backache (5 yrs)</td>
<td>T-10</td>
<td>marginal excision</td>
<td>lost to follow-up</td>
</tr>
<tr>
<td>5</td>
<td>M, 58</td>
<td>intermittent low backache (15 yrs), progressive stiffness (3 mos)</td>
<td>C-2 &amp; C-3</td>
<td>marginal excision</td>
<td>NED (9 yrs 4 mos)</td>
</tr>
<tr>
<td>6†</td>
<td>M, 32</td>
<td>epileptic attacks (12 yrs)</td>
<td>brain (frontal lobe)</td>
<td>wide excision</td>
<td>NED (30 yrs)</td>
</tr>
<tr>
<td>7†</td>
<td>F, 45</td>
<td>history of multiple cranial nerve involvement (12 yrs)</td>
<td>skull base (rt sphenoid, occipital bone, sella, foramen magnum), involvement of cranial nerves &amp; nasopharynx</td>
<td>none</td>
<td>autopsy</td>
</tr>
<tr>
<td>8†</td>
<td>M, 58</td>
<td>progressive hoarseness &amp; decreased hearing (3 yrs)</td>
<td>skull base (jugular foramen)</td>
<td>intralesional excision</td>
<td>lost to follow-up</td>
</tr>
<tr>
<td>9†</td>
<td>M, 12</td>
<td>neck stiffness &amp; pain (1 mo)</td>
<td>C-6</td>
<td>curettage</td>
<td>NED (3 yrs 3 mos)</td>
</tr>
<tr>
<td>10†</td>
<td>M, 32</td>
<td>back pain (&quot;many years&quot;), spina bifida</td>
<td>L-4 &amp; L-5</td>
<td>intralesional excision</td>
<td>NED (7 yrs)</td>
</tr>
<tr>
<td>11†</td>
<td>F, 33</td>
<td>mid-back pain (3 mos)</td>
<td>T-9</td>
<td>intralesional excision</td>
<td>lost to follow-up</td>
</tr>
<tr>
<td>12†</td>
<td>F, 68</td>
<td>pain rt hip (5 mos)</td>
<td>L-4 &amp; L-5</td>
<td>marginal excision</td>
<td>degenerative joint disease in lumbar region (16 mos)</td>
</tr>
<tr>
<td>13†</td>
<td>F, 20</td>
<td>incidental finding (enlarging mass)</td>
<td>C-2</td>
<td>curettage</td>
<td>lost to follow-up</td>
</tr>
<tr>
<td>14†</td>
<td>F, 56</td>
<td>back pain</td>
<td>L-4 &amp; L-5</td>
<td>curettage</td>
<td>lost to follow-up</td>
</tr>
</tbody>
</table>

* NED = no evidence of disease.
† Patients referred for consultation.

the soft tissue adjacent to the spinal cord, mainly at the intervertebral disc level, in an epidural location. Three of these lesions were associated with abnormalities of the bone.

Clinical Findings

Nine of the 14 patients complained of pain, which had been present from 1 to 5 months in five and from 5 to 23 years in three. The duration of pain in one patient (Case 10) was not specified, but it had been present for "many years." Neurological symptoms included epileptic attacks in Case 6, involvement of multiple cranial nerves in Case 7, progressive hoarseness in Case 1, and diminished hearing in Case 8. These symptoms were present from 3 to 12 years in two patients and for "many years" in one. In one patient (Case 13), the lesion was discovered fortuitously on radiographs performed because the patient had been injured in a skiing accident.

Radiographic Findings

Radiographs were available for evaluation in nine of the 14 cases. The mass was seen at the skull base in five of these cases, and in the frontal region in one. In three cases, the lesion was intraspinal. In these three cases the mass was seen in an extradural location at myelography. In two, the symptoms were considered likely to be due to extrusion or herniation of intervertebral disc mate-

Fig. 1. Graph showing age and sex distribution of 14 patients with calcifying non-neoplastic lesions of the neural axis.
rial, with defects located anterolaterally. Myelography or computerized tomography (CT) showed evidence of calcification in both of these cases. In the third case, the lesion was located posteriorly in the lumbar region and was closely associated with a facet joint. Evidence of calcification in this lesion was also seen on CT. The most likely diagnostic possibility in this case was a calcified synovial cyst of the lumbar facet joint (Fig. 2).

In five of the six cases in which the head was involved, radiographs showed the lesion to be adjacent to the foramen magnum (Fig. 3). In two cases, the mass extended inferiorly and could be visualized as a retropharyngeal soft-tissue mass (Fig. 4). All five lesions seemed to arise in extraosseous tissues, but there was evidence of bone erosion in three of them (two showed erosion of the petrous ridge and one showed extensive involvement of multiple bones including the clivus). Calcific deposits were identified in the mass by either radiography or CT in four of these five cases. The differential diagnosis included chondroid chordoma and acoustic neuroma. In the remaining case involving a lesion in the head, the lesion was located in the frontal lobe of the brain. Plain films and tomograms showed only reactive sclerosis of the orbital roof, as might be seen with meningioma. The mass was not visualized.

**Pathological Findings**

Grossly, all lesions were a grayish-yellow mass between 1 and 10 cm in diameter, and 11 of them contained calcium. One lesion was very fluid and resembled pus. Two lesions were extensive, involving many bones of the base of the skull. The gross appearance of one, which involved the C-2 vertebra, was suggestive of an osteoblastoma.

The histopathological appearance of the surgical material was similar for the lesions; the only variation consisted of the different distribution of the various components, which were epithelioid cells (some spindling) and giant cells (palisading around amorphous, chondroid, or calcifying material). The arrangement of the cellular components was typically in granulomatous fashion (Fig. 5 left). In five cases, these granulomas were large and confluent and showed a lobular configuration. In six cases the granulomas were clearly delineated, with no blending between them (Fig. 5 center). In the final three cases, this nodular pattern coexisted with the previously described lobular pattern. The nod-

![Fig. 2](image1.png)  
**Fig. 2.** *Left:* Myelogram of the lumbar region, lateral view, showing a large posterior extradural defect at the level of the facet joint between L-4 and L-5. *Right:* Computerized tomography scan showing a mass at the level of the right facet joint between L-4 and L-5. There is some calcification in the rim of this soft-tissue mass.

![Fig. 3](image2.png)  
**Fig. 3.** *Upper:* Tomogram of the foramen magnum, lateral view, demonstrating a calcifying mass within the foramen magnum. *Lower:* Computerized tomography scan localizes the calcifying mass to the right side of the foramen magnum.
ular component, whether occurring as separate nodules or showing confluence, had the same morphological appearance. It was possible to identify a peripheral and a central zone. The latter was made up of a nondescript material consisting of calcification in granules or in linear arrangement (like chicken footprints), along with a hyaline, basophilic material with a chondroid appearance. Very few cells were identified in those areas, although sometimes there were only some “ghost cells.” The hyaline, basophilic, chondroid, calcifying masses were arranged in large plates or fragmented in small pieces (Fig. 5 right). Along the border of the masses, there was a fence-like proliferation of round-to-oval spindling epithelioid cells. These cells were plump with prominent, deeply staining (mainly cosinophilic) cytoplasm with clear-cut borders. The prominent nuclei were at the center of the cells or near the cytoplasmic membrane. The cells were “palisading” around the basophilic masses, some of which were calcified. Large multinucleated giant cells were identified along with these cells, which had epithelioid features. In two cases a granuloma-like arrangement of “epithelioid” cells and giant cells without hyaline, calcifying, chondroid material was identified along with the features described above. Calcification in the form of extensive large granules or in fine dust particles was present in all 14 lesions. In three cases, the hyaline, basophilic material merged with lamellar bone. With the polarizing lens, the birefringence of the collagen bundles in the bone stopped at the edge of the hyaline, basophilic, calcifying masses.

In two of the intraspinal cases, the basophilic calcifying material resembled the hyaline material of the intervertebral disc. Among the lobules or nodules, different quantities of fibrocellular stroma were identified. In 12 cases the stroma was mainly fibrovascular; scattered lymphocytes were seen in nine of these. In two cases the stroma was made up of acellular collagen and few vessels. In eight cases a rich fibroblastic proliferation

Fig. 4. X-ray film, lateral view, of the skull showing a large retropharyngeal soft-tissue mass, which contains some calcific deposits.

Fig. 5. Photomicrographs of surgical specimens. Left: Hypocellular but confluent granulomas are seen with prominent palisading of epithelioid at margins of the granulomas. Note the dark areas indicating foci of calcific deposits in some of the granulomas. H & E, x 60. Center: Clearly delineated granulomatous nodules are visible. There are round-to-oval epithelioid cells and giant cells proliferating around irregular masses of calcified basophilic material. Vascular connective tissue and a few round cells separate the granulomas. H & E, x 95. Right: The central zone of a nodular lesion shows epithelioid cells intermixed with fibrillar, sometimes calcifying matrix. Note the chondroid aura near the center. Scattered lymphocytes are also present. H & E, x 150.
of spindle cells was seen. Brown hemosiderin pigment was clearly identified in four cases.

The lesions in the frontal lobe of the brain as well as in the cerebellar tonsil had the same histological appearance as described above (Fig. 6 upper pair). Bone involvement was identified histologically in seven cases (Fig. 6 lower pair). In one case, it was not clear whether the few islands of lamellar bone present in the specimen were reactive bone or new bone produced by the lesion. Material for culture was obtained in two cases and was negative in both cases.

Treatment and Survival

Information about treatment was available for all but one tumor, which was found at autopsy. Two patients had undergone wide excision for a lesion located in the brain. Of the 11 other patients, one had had a “debulking” procedure, seven had been treated with intraleisional excision or curettage, and three had undergone marginal excision. Only one patient had suffered a recurrence (3 years after an “incomplete excision”), and intraleisional debulking was performed. The lesion was extensive, involving multiple bones of the skull base, the posterior wall of the nasopharynx, the left cerebellopontine angle, and the left jugular foramen. This patient died in coma following a cerebrovascular accident 13 years after the operation. Five patients were lost to follow-up review. For the remaining seven patients, the follow-up period was 16 months to 30 years (average 10 years). With the exception of the patient
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who died 13 years after surgery and the case reported at autopsy, all patients were alive at the last follow-up review. Eleven patients had no evidence of disease, and one had significant degenerative disease.

Discussion

The radiographic differential diagnosis of these calcifying lesions is diverse, depending on the location. For lesions at the base of the skull with bone involvement, the possibility of chordoma or chondroid chordoma has to be considered, especially when the lesion is centrally located. Chondrosarcoma and chordoma are two other possibilities. When the lesion is located along the spinal canal, the most likely possibilities are herniated disc material and synovial cyst, depending on location.

If the lesions are in the soft tissue adjacent to the brain or in the cerebellopontine angle, the possibility of a neoplastic or a non-neoplastic lesion has to be considered. In the neoplastic group, meningioma, craniopharyngioma, and some teratomas and dermoid cysts may show evidence of calcification. Calcification is more common in meningiomas that are located along the spinal cord; when calcification is prominent, the lesion is called a “psammomatous meningioma.” In rare instances, neurofibroma and schwannoma contain calcific foci. Of the non-neoplastic lesions that show evidence of calcification, cerebral calculi (“brain stones”) and hematoma with foci of mineralization have to be considered. Calcific deposits may also be present in an aneurysm or an arteriovenous malformation in the base of the brain. Calcific deposits may also occur in tuberculosis as well as in multiple masses in tuberous sclerosis.

Among lesions arising in the soft tissue and adjacent to the spinal cord, a herniated disc and a synovial cyst are the most likely possibilities. Psammomatous meningioma, neurofibroma, schwannoma, and calcifying tuberculosis may also be considered. The lesion in the substance of the brain must be differentiated from a primary calcified brain tumor such as astrocytoma, oligodendroglioma, choroid plexus papilloma, and ependymoma.

The histological appearance of this non-neoplastic lesion is characteristic, as it is composed of discrete or confluent granuloma-like masses. Prominent palisading epithelioid cells surround zones in which amorphous calcifying material, usually with a chondroid appearance, is seen. This histological appearance allows the lesion to be distinguished in the differential diagnosis. Microscopically, the main differential diagnosis involves chordoma, chondrosarcoma, chondroblastoma, and infectious granulomatous disease. These lesions share with chordoma the lobular configuration and the chondromatous appearance. But the appearance of the cells and their arrangement are completely different. Chordoma has ribbon-like cells arranged in otherwise abundant extracellular matrix. The cells of a chordoma may have an epithelioid appearance, but the hallmark is the vacuolated pattern of the cytoplasm. “Physaliferous” cells were not present in the lesions in our series. The cartilaginous aura may be suggestive of chondrosarcoma, and the calcification, as well as the epithelioid cells, makes one consider chondroblastoma; however, neither of these two lesions has a nodular or confluent granulomatous configuration. Tuberculosis must be ruled out, but the lesions in our series did not have the peculiar necrosis or the consistent lymphocytic infiltration around the granuloma seen in tuberculosis. Langhans’ giant cells were not identified in any of the lesions in our series. In lesions of the spinal column in which the amorphous calcifying material simulates osteoid or shows bone production, osteoblastoma and osteosarcoma are other possible diagnoses.

The nature of the process is unknown. Similar cases were described by Rhodes and Davis, who reported seven cases and stated that there was an unusual fibro-osseous component in the intracranial lesions. Six of their lesions were incidental findings at autopsy. Three of these six lesions were multiple dural nodules, one was a mass attached to the inferoposterior medial aspect of the left cerebellar hemisphere, and two were associated with the choroid plexus stroma in one of the Luschka foramina (one case) and in the leptomeninges around the pineal body (one case). The seventh case was that of a 27-year-old woman with worsening daily bilateral headaches who was referred for a surgical consultation. On radiographs of the skull, calcific deposits were noted overlying the right orbital roof. Cranietomy revealed a mass in the right frontal lobe but no dural involvement. The firm gray-white mass was 6 × 4 cm. A marginal excision was performed. The patient was without evidence of disease 7 years later.

Jun and Burdick described a 55-year-old man whose main complaints were dizziness, headache, and vomiting. They used the term “an unusual fibro-osseous lesion of the brain.” Radiographs of the skull and a CT scan showed a calcific mass 3 cm in diameter. The mass was much larger than that seen on the skull radiographs taken 8 years previously after a minor concussion. At right frontoparietal craniotomy, a mass resting on the corpus callosum and surrounding the right pericallosal artery was identified and marginal excision was performed. The mass had a flaky outer shell and a core of hard osseous material. The authors did not mention the length of the follow-up period, but they specified that the postoperative course was benign.

We are not aware of any other cases reported in the literature, but we have observed similar lesions in the extraneural axis of three patients who were excluded from the present series. One patient had a lytic lesion in the neck of the left radius with cortical bone violation and soft-tissue extension, one had a lesion in the soft tissue at the base of the first finger, and one had a lesion in the roof of the right orbit. Five years after tumor excision, the first patient had no evidence of disease. The second patient died of unrelated causes 13 years
after excision of the mass, never having had recurrence of the lesion. The third patient had curettage and was lost to follow-up review. In these three cases, the pathological findings were the same as those described in the neural axis in this report.

The lesion was benign in the cases in this series, as well as in the few cases reported in the literature. After wide or marginal excision, the prognosis was very good; after intrallesional excision and debulking, the prognosis was usually excellent. Only one patient in our series (Case 1) had a recurrence after intrallesional excision; he was treated again with intrallesional debulking and eventually died from cerebrovascular disease 13 years later. This patient had had a very extensive lesion at the base of the brain with invasion of multiple bones. In another of our cases (Case 7) a very extensive lesion at the base of the brain with multiple bone involvement was found at autopsy. In spite of these two cases, we believe that this lesion is a benign, non-neoplastic, possibly reactive proliferative process and is probably an unusual expression of tumoral calcinosis. The usually good clinical result, even if the lesion is not completely extirpated, suggests that the lesion is non-neoplastic. The granulomatous appearance favors a reactive proliferating process. The fact that in two cases death was apparently caused by the tumefaction emphasizes that, if strategically located, the lesion may result in a fatal outcome.

References

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